

## Research Needs Identified for Endocrine Disruptors

Research Area	Research Need
Basic Research	Dissection of direct immune–endocrine interactions Understanding of cellular and molecular mechanisms Sensitive, inexpensive, and widely available analytical tools Understanding the biological significance of subtle low-dose effects Identify and characterize critical windows of susceptibility across species Characterize source of population heterogeneity in dose responsiveness (age, gender, nutrition, etc.)
Exposure Determination	Rapid and inexpensive exposure monitoring methods for use in wildlife populations Increased monitoring efforts to identify status and trends of EDs Environmental causes of liver, brain, and lung cancers
Mixtures	Research to address the additivity principle for mixtures <i>In vitro</i> and <i>in vivo</i> studies of complex mixtures to evaluate validity of TEQs Identification and testing of environmentally relevant mixtures Systematic evaluation of species, cellular, and age dependent response to mixtures of EDs
Multidisciplinary Studies	Systematic field and laboratory studies focused on critical uncertainties Examination of correlation of effects between wildlife and mammalian models Multidisciplinary studies on effects of endocrine disruption Examination of multiple endpoints and multiple tests of ED action
Risk Models	Statistical models to predict risk from exposure and effects Improvements in study design Evaluation of toxicity and mechanistic endpoints across species Toxicokinetics and toxicodynamic studies of environmentally relevant chemicals Quantitative dose response models based upon receptor theory/biochemical interactions Establishment of training programs in biomathematics for BBDR model construction

**Source:** Adapted from Kavlock RJ et al., Research needs for the risk assessment of health and environmental effects of endocrine disruptors: a report of the U.S. EPA-sponsored workshop. *Environ Health Perspect*, 104(Suppl 4):715–740 (1996).

“Although trends in hormonally related diseases have not been clearly linked to environmental chemicals, it is probable that endocrine disruptors are contributing to human diseases and dysfunction. The question then becomes how much they are contributing,” Lucier said. “What is needed is high-quality basic and applied research to examine a number of critical areas.”

Many individual federal agencies have been working to develop research needs and priorities. In April 1995, the EPA sponsored an interdisciplinary workshop on the human health and ecological effects of endocrine disruptors to identify research gaps and determine future research priorities. According to the workshop summary, attendees concluded that research should focus primarily on effects on development of reproductive capability, on improved exposure assessment, and on the effects of mixtures. (See conference summary report, *Environmental Health Perspectives*, August 1996.)

The goal of the CENR working group is to evaluate and harmonize the needs and

priorities of the various agencies. Lucier says that an interagency approach is important to the development of a national strategy. “The most effective way to utilize basic research to make sound policy decisions is to develop interagency approaches that maximize its application to multiple agencies,” he said. “We will develop cross-cutting approaches useful to all agencies.” An interagency approach also maximizes communication, Lucier added.

The CENR group has worked to put together a document prioritizing federal research needs. According to a preliminary draft of the strategy, the highest priority is determining the effects of endocrine disruptors on developing organisms, particularly on

the reproductive system. Other priorities include assessing the potential carcinogenic effects and the toxicology of mixtures and assessing the nature and extent of contamination in the area of exposure. The group is also working to develop a comprehensive evaluation of all federally funded research projects on endocrine disruptors. According to Lucier, the group will also focus on how to link scientific activities to public policy decisions. The strategy is due out in September.

## Rewarding Cancer Research

Alfred G. Knudson, Jr., and Joseph F. Fraumeni are this year's recipients of the Irving J. Selikoff Award for Cancer Research. Knudson and Fraumeni earned the award specifically for “research on the molecular origins of cancer and its application to the management of populations at high risk,” said Sheldon Samuels, vice president for policy studies at the Ramazzini Institute, which was founded by Selikoff to promote occupational and environmental health research. The Ramazzini Institute sponsors the annual award.

Selikoff, who died in 1992, is remembered for his work at New York's Mt. Sinai School of Medicine in linking cancer and other diseases with environmental pollutants such as asbestos. The award consists of a plaque and a monetary prize given from a fund developed by Selikoff at the Ramazzini Institute. “We decided to keep the fund alive,” Samuels said, adding that the fund is entirely privately endowed. The award is given to scientists who demonstrate excellence in expanding genetic research on how to repair cancer-causing damage—to prevent cancer from later appearing even though people have been exposed in the past. The award recipients are selected by a panel of officers at the Ramazzini Institute.



**Selikoff standouts.** Alfred G. Knudson, Jr. and Joseph F. Fraumeni (left to right holding boxes) are the 1996 winners of the Irving J. Selikoff Award for Cancer Research. They are flanked by Philip Landrigan (left) and Arthur C. Upton (right) of the Mt. Sinai School of Medicine.



## Food, Drugs, and More

One-fourth of the money spent each year by Americans is spent on products regulated by the U.S. Food and Drug Administration; this amounts to over \$1 trillion worth of goods—from eyeshadow to AZT—that must meet FDA guidelines for product safety and quality. Currently, all foods and drugs (for both animals and people), cosmetics, and radiation-emitting equipment are FDA regulated, and the agency seems poised to add the \$2.8 billion tobacco industry to this list. From proposing tobacco regulation to researching the effects of the “morning after” pill, this obligation requires that the FDA study and debate some of the most divisive issues facing the nation. Part of the continuing dialogue between the FDA and the public consists of the agency’s home page, located at <http://www.fda.gov/fdahomepage.html>, the entranceway to a well-designed resource on FDA programs and regulations.

From the home page, a user can choose one of eight icons to link to the home pages of specific FDA programs, read the FDA news, or change to another directory. Despite the aesthetic appeal of the site, however, the complex structure of the FDA can make it difficult to find the particular information being sought. The FDA search engine, which can be accessed from the bottom of the home page, offers another way to find FDA documents on specific subjects. Also located on the home page is a Comments link that allows users to correspond with the FDA via electronic mail.

Through the FDA News link, users can find information such as the text of proposed tobacco regulations and guidelines for protecting children from lead poisoning. The results of recent research studies are also presented here along with current press releases and product recalls (under the Latest FDA Enforcement Report link). This site also offers a calendar of upcoming meetings and symposia and a searchable archive of past press releases, papers, testimonies, reports, articles, and major speeches. Another link brings up the latest issue of *FDA Consumer* magazine, with full text of articles and back issues.

The Foods icon links users to information from the Center for Food Safety and Applied Nutrition, along with external biology-related resources that can be accessed from the CFSAN page via the Info link. Other links connect users to consumer advice on food handling, information on food additives like olestra and MSG, and facts about foodborne illnesses. The Bad Bug Book, which can be found under the Foodborne Illness link, provides descriptions of common pathogens as well as information about disease outbreaks and symptoms.

The Center for Drug Evaluation and Research site, linked through the Human Drugs icon, is evolving into a comprehensive resource on drug composition and regulation. Information on how the FDA screens new drugs, approves them for market, and ensures accuracy in testing, formulation, and labeling can be reached from the CDER home page by selecting the About CDER icon and following the Office of Compliance link to the Annual Report FY 95. Also within the annual report are pages on FDA drug recalls and a directory that lists FDA personnel by their area of expertise. The Division of Over-the-Counter Drug Products maintains lists of drug name changes and will soon host a complete database of active drug ingredients. The Drug Info icon on the CDER home page brings users to a list of approved drug products with therapeutic equivalence evaluations along with descriptions of drugs that have been approved in the last three years. Guidance documents for the drug manufacturing industry can be reached from the CDER home page via the Regulatory Guidance link.

The links to other FDA programs—Biologics, Devices and Radiological Health, Animal Drugs, Cosmetics, Field Operations and Imports, and Toxicology—all provide data pertinent to those particular fields. For instance, the Center for Biologics Evaluation and Research (Biologics link), which oversees the manufacture and sale of vaccines and blood products, provides a link to the Vaccine Adverse Response Reporting System. The Center for Devices and Radiological Health provides a useful list of safety alerts and advisories under the Program Areas link, and the National Center for Toxicological Research can be reached through the Toxicology icon.



Knudson, a researcher at the Fox Chase Cancer Center in Philadelphia, Pennsylvania, was chosen for his research on developing models of carcinogenesis. “He is not only a great laboratory scientist, but he happens to be a conceptualizer, a theoretical biologist whose models of carcinogenesis are the basis of much of the research on the interface between the environment and our genetic inheritance,” Samuels said. “Knudson was one of the conceptual pioneers who discovered the family of genes associated with retinal glaucoma, which is important in understanding cancer in general, because this same family is important in other cancers.”

Fraumeni, who is director of the Division of Cancer Epidemiology and Genetics at the National Cancer Institute (NCI) in Bethesda, Maryland, was given the award for his research in environmental and genetic factors in cancer, and in clarifying the role of genetic susceptibility.

According to Samuels, one of Fraumeni’s most significant accomplishments has been the development of a program at the NCI in genetics and epidemiology. The program, links molecular biology, epidemiology, and prevention. “We are just now beginning to see the fruits of [Fraumeni’s] work,” Samuels said. “He deserves to be recognized for his achievement in pulling that program through.” The awards were presented 21 May 1996 at the Mt. Sinai School of Medicine. “It’s a great honor,” said Fraumeni. “Both Dr. Knudson and I were delighted to receive the award given in memory of Dr. Selikoff, who contributed so much to the area of environmental cancer research.”

## New Evidence on Sperm Counts

In 1992, a Danish research team led by Niels Skakkebaek at the National University Hospital in Copenhagen published the results of a meta-analysis of sperm count studies covering 50 years. The team concluded that human sperm counts had declined by as much as 50% during that time. Since then, many environmentalists, journalists, and reputable scientists have relied on this study to assert that environmental toxins are having an adverse effect on male fertility. Of special concern are both natural and manmade compounds called endocrine disruptors.

Three reports in the May 1996 issue of *Fertility and Sterility* challenge the assertion that sperm counts are declining worldwide. Sperm quality is measured by